Kerry Leifer General – 6/24/2021

Agenda

Ex. 5 Deliberative Process (DP)

Acute Toxicity

- Inpyrfluxam Acute Tox and CDPR/Valent issue—discussed 5/27, meeting with FB 0n 6/15 to prepare response (see pg 3-4 below)
- Process improvements for review assignments and scheduling –Timeline for reviews from date of receipt in CITAB (both PC and AT) discussed with subgroup of PMWG.
- Development of Acute Tox Priority Spreadsheet for RD
- "more examples of problems caused by EPA incompetence and corporate malfeasance" email – response sent by Paul DiSalvo with technical assistance from Julie Breeden-Alemi.
- Substantial Similarity – actions coming to CITAB with >1 cited similar product (in one case 67 MRIDs cited)—not consistent with category and past practices—to be discussed at PMWG
- "Mission Critical"—request from PHS employee

Inert Ingredients

- Propylene glycol and Ray McAllister/CLA et al proposal. Phase 1 letter issued 5/3. Phase 2 letter drafted and circulated for comment 6/7, comments received and addressed. Revisions made (including per M. Goodis 6/16 email) and updated document circulated 6/17. No further feedback has been received.
- PFAS

Ex. 5 Deliberative Process (DP)

- Commodity Inert Ingredients. Requests for further additions—request from HCPA.
- Fragrance tolerance exemption petitions—Pat Quinn inquiries—team has developed action plan—response provided to Julie Timberman/Clorox—Biweekly "check-in" meeting with Pat&Julie started 6/14. Per meeting today with David and Mohamed G. we should have RA document and draft FR ready to go to OGC by week of 7/5.

- Inert Team has developed detailed spreadsheet of all pending inert actions with eye to efficiencies in assignments/roles
- Bullets of steps being taken to address inert petition backlog has been drafted
- Inert Ingredient Branch Box – customer expectations vs resources—added auto response language
- Microbial inert ingredients and role of BPPD –Seiichi identified as contact by Catherine (THANK YOU)

Product Chemistry

- Self-Certification—still awaiting OGC response to PR 98-1 certification statement—Allison Payne emailed 2/4
- ACB PC reviewer process continues - assignments made in conjunction with June prioritization
- SWAT TEAM – 2 FHB reviewers, one HB reviewer (started week of 3/8), one IVB2 (NOWCC) reviewer)
- PFAS—review of Clarke products. First batches of reviews completed. Additional actions now in queue—two Clarke actions to be completed 6/7—actions completed, checking with IVB 1 to verify if there are any outstanding actions.
- RAB8—kickoff meeting held 5/25—initial assignments provided to RAB 5/26. Follow up meeting held 6/9 (OPPIN/Documentum training), review of initial assignments 6/17. First two reviews have been prepared by RAB 8 and are undergoing secondary review. Additional 8 assignments given to RAB 8

Other CITAB issues/activities

- PFAS—Results of substructure search for PFAS in active ingredients
- CITAB Office hours—next session to be scheduled for week of 7/5
- Meeting w/ Bo on 6/28 to discuss strategy around tiger team starting to be assigned CSF actions.
- Additional funding for contractor—completed. Per resources discussion would further extramural funding for additional RD/CITAB work be a consideration for current contract or next contract?
- CSF Images and Documentum/ITRMD
- CITAB staff questions/concerns regarding telework and GFE (monitors, etc.)

[1] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/acute-oral-toxicity-and-down-procedure

Dear Ms. Giles-Parker and Ms. Garvie,

Valent U.S.A. LLC has two new product registrations pending with CDPR that were submitted November 2019: S-2399 2.84 SC Fungicide, EPA Reg. No. 59639-230 (Excalia® Fungicide), and S-2399 3.2 FS Fungicide, EPA Reg. No. 59639-231 (Zeltera® Fungicide).

The data packages for these formulations have been reviewed by the US EPA and registration was granted in August 2020. As part of the data packages, a complete set of acute toxicity studies was submitted in support of the registration. The results are described in the tables below.

Following submission of these same data packages to the CDPR for review and approval, CDPR disagreed with the conclusion of the US EPA's interpretation of the acute oral toxicity study (MRID 49706201) for S-2399 2.84 SC Fungicide, 59639-230 (Excalia® Fungicide). The CDPR reviewer determined the LD_{50} was 175 mg/kg, Category II for acute oral toxicity.
The acute oral toxicity study was conducted using the Up-Down technique in conjunction with the Acute Oral Toxicity (Guideline 425) Statistical Program (Westat, version 1.0, May 2001), as recommended by the US EPA [1]. The conclusion of the study report, as reflected by the EPA's Data Evaluation Report (DER), is an LD_{50} of 550 mg/kg. Study results are captured in the table below

CDPR's interpretation of the study results were more conservative and determined the rat oral LD_{50} was 174 mg/kg, toxicity category II. The justification for this conclusion is as follows; "It is this HHA reviewer's contention that due to the paucity of the study results, a conservative interpretation is in order. **Simply the fact that 2 of the 3 animals died when dosed with 550 mg/kg would preclude establishing the LD50 value at 550 mg/kg.** In the probit analysis of dose-response data, the slope of the curve dictates the calculated LD50 value. In this instance the data are so minimal that such an assessment is not possible. **Therefore, it was concluded that the Category II hazard was appropriate for this product in the light of the submitted data**."
The discrepancy in conclusions by the US EPA (LD_{50}=550 mg/kg, Category III) and the CDPR (LD_{50}=174 mg/kg, Category II) presents a conflict and poses critical issues for Valent in terms of labeling and use patterns. The EPA approved the label for S-2399 2.84 SC Fungicide which currently complies with safety and precautionary statements consistent with Category III acute oral toxicity results. If CDPR's conclusion is finalized, Valent will have to amend the label at USEPA to reflect CDPR's recommendation. It is not practical nor feasible to have separate labels for California and the rest of the US. The alternative is to revert to testing techniques that use a large number of animals, which is unacceptable

and is in direct opposition to the EPA's recent proclamation to reduce animal testing by 30% by 2025 and completely by 2035[2]. Furthermore, the up-and-down method using the AOT425 Statistical Program is acceptable for the Series 870 Health Effects Test Guidelines for acute toxicity testing and by the Organisation for Economic Co-operation and Development member nations.
Therefore, Valent is seeking advice from the EPA to rectify the issues created by CDPR's interpretation of the acute oral toxicity study. We would like to ask several questions regarding the issue:

- • Has the EPA encountered similar examples where CDPR had different interpretations for acute toxicity studies? If so how did the Agency address these differences?

- • What are the Regulatory ramifications of having label precautionary statements consistent with toxicity category III for Federal labels while having more precautionary statements on California labels?

- • What options do we have as a company to address these discrepancies in scientific conclusions between Federal and State Agencies?